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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/853,646	05/14/2001	Nicholas C. Nicolaides	001107.00138	6480
22907	7590	11/19/2003	EXAMINER	
BANNER & WITCOFF 1001 G STREET N W SUITE 1100 WASHINGTON, DC 20001			SHUKLA, RAM R	
			ART UNIT	PAPER NUMBER
			1632	

DATE MAILED: 11/19/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

<p align="center">Office Action Summary</p>	Application No. 09/853,646	Applicant(s) NICOLAIDES ET AL.	
	Examiner Ram R. Shukla	Art Unit 1632	

-- Th MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 21 July 2003.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-50 is/are pending in the application.
- 4a) Of the above claim(s) 8-50 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-7 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 14 May 2001 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
 If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
 a) ☐ All b) ☐ Some * c) ☐ None of:
 1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
 * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
 a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

1. Applicant's response and amendments filed 7-21-2003 are acknowledged.
2. Amendments to claims 1, 6 and 7 have been entered.
3. This application contains claims 8-50 drawn to an invention nonelected with traverse in Paper No. 17. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.
4. Claims 1-7 are under consideration.
5. The written description and enablement rejection of claims 1-7 have been withdrawn in view of the applicants' amendments and arguments.

Claim Rejections - 35 USC § 112

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 6 and 7 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 6 is indefinite because it recites dominant-negative allele of any mismatch repair gene however the independent claim, claim 1, limits the mismatch repair gene to PMS2. Therefore, the metes and bounds of the claimed invention are not clear.

Claim 7 is indefinite because it depends from claim 6.

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

9. Claims 1-7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nicolaides et al 1998 Molecular and Cellular Biology 18:1635-1641) or Nicolaides et al (US Patent 6,146,894, 11-14-00, effective filing date 4-14-1998) in view of Bujard et al (WO 96/01313, 1-18-1996) for reasons of record set forth in the previous office action of 3-19-03.

Response to Arguments

Applicant's arguments filed 7-21-03 have been fully considered but they are not persuasive. Applicants' argue that none of the cited references provide any suggestion to make the claimed invention. Applicants further argue that Bujard only teaches the desirability to use tetracycline-regulated gene expression system to turn of expression of genes that are cytotoxic to cell lines and that PMS-2 dominant negative is not cytotoxic. However applicants' arguments are not persuasive because while PMS-2 is not cytotoxic in a literal sense, since it causes hypermutability to a cell, which results in cancer formation, which is not desirable, it will be harmful to a cell. Additionally, the Bujard reference does not merely teach their system to use in case of cytotoxic cells, but the system can be used in any situation where one would like to produce a protein or stop its production and in the instant case, an artisan would have liked to control the expression of a protein that makes a cell hypermutable. Next, applicants argue that in view of the amendment of the claims to recite in vitro methods, the rejection is not proper because cells growing in vitro do not cause cancer. Again these arguments are not persuasive because the argument that cells grown in vitro do not cause cancer is not correct since transplantation of cells in mice to produce tumors is well known and therefore cells grown in vitro can cause cancer. Furthermore, the issue is not causing cancer;

rather it is a method of generating mutation by expressing dominant-negative allele of PMS2 in a cell where the expression of the PMS2 gene is regulated, which is obvious to make with a reasonable expectation of success in view of the combined teachings of the cited references. Therefore it is reiterated that at the time of the invention, it would have been obvious to one of ordinary skill in the art to modify the expression vector of Nicolaides et al for expressing the dominant negative mutant of PMS2 as taught by Bujard et al with a reasonable expectation of success. An artisan of skill would have been motivated to use the expression system of Bujard et al because it would have provided a regulated expression of the dominant negative PMS2 and such would have been desired because the continuous expression of the dominant negative PMS2 would have resulted in high rate of mutation in the genomic DNA of the cell resulting in transformation. It is noted that the dominant negative PMS2 expression was known to cause cancer at the time of the invention.

10. No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

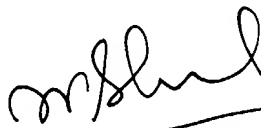
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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ram R. Shukla whose telephone number is (703) 305-1677. The examiner can normally be reached on Monday through Friday from 7:30 am to 4:00 p.m. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah Reynolds, can be reached on (703) 305-4051. The fax phone number for TC 1600 is (703) 703-872-9306. Any inquiry of a general nature, formal matters or relating to the status of this application or proceeding should be directed to the William Phillips whose telephone number is (703) 305-3413.

Ram R. Shukla, Ph.D.

Primary Examiner

Art Unit 1632


RAM R. SHUKLA, PH.D.
PRIMARY EXAMINER